

**REMARKS/ARGUMENTS**

By this Amendment, claims 3, 6, 10, 13 are amended. Claims 1-14 are pending.

Citations to the Specification are directed to U.S. Patent Application Publication No. 2005/0154052 (Parthasaradhi et al.)

Support for the amendments to the claims can be found throughout the Specification as filed, and specifically: support for the limitation in claim 3 for heating the mixture to reflux and cooling to about 20°C can be found on page 2, ¶[0017]; support for the limitation in claim 6 for the step of maintaining the mixture at about 30 minutes for 0°C can be found on page 2, ¶[0018]; support for the limitation in claim 10 for the step of maintaining the mixture at about 40°C for about 30 minutes, then cooling at about 0°C can be found on page 2, ¶[00190]; support for the limitation in claim 13 for the step of maintaining the mixture at about 40°C for about 30 minutes, then cooling at about 0°C can be found on page 2, ¶[0020].

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

**Rejection under 35 USC 102(b)**

Claims 1-2 stand rejected under 35 USC 102(b) over U.S. Patent No. 4,943,590 (Boegesoe et al.). This rejection is respectfully traversed.

The Examiner sets forth that the prior art disclosed a crystalline (+)-citalopram crystallized from acetone. The Examiner argues that the instant claimed (s)-citalopram oxalate was prepared in the same manner using acetone as the solvent, and that since a product cannot be separated from its physical property, therefore, the limitation of claims 1-2 are innate nature and inherent anticipation was found.

The Examiner alleges that Applicants do not offer any evidence that the instant material is a "different material" which is prepared by non-acetone solvent or any factual evidence that the acetone crystallized material of the instant examples 1, 2 or 5 are different from the prior art since an allegedly identical process was employed.

However, while the '590 patent discloses crystallization from acetone (see e.g. Example 2), the instant application discloses that (S)-citalopram oxalate is mixed with acetone, heated to reflux and is cooled to 20°C, then the separated crystals are filtered (see ¶[0017] Example 1). As set forth in the Response filed February 12, 2009, the Banga reference teaches that different

crystalline modifications arise under varied experimental conditions, including, inter alia, thermal treatment. Therefore, the assumption that crystallization using distinct thermal profiles and solvents has no basis in fact.

Accordingly, the art teaches that XRPD data is reliable to differentiate between different polymorphic crystalline forms. Applicant has provided XRPD data for the claimed polymorphic form of citalopram oxalate, and demonstrated that the form as taught in the '590 patent is distinct from the claimed polymorphic form.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

**Rejection under 35 USC 112 first paragraph**

Claim 1-2 and 3-7 stand rejected under 35 USC 112 first paragraph as allegedly lacking enablement. This rejection is respectfully traversed.

The Examiner sets forth that where applicants argued that claims 1-2 is a different material prepared from non-acetone solvent then, the new matter rejection is still applicable and notes that the only Form I prepared in examples 1, 2 and 5 are from acetone. The Examiner argues that the exclusive disclosure of acetone as the sole solvent for preparing form I (S)-citalopram oxalate is tantamount to a teaching away from using any other solvent absent of factual support.

The Examiner sets forth that in view of the exclusive operability limiting to making form I using acetone only, a 112 first paragraph rejection of enablement is maintained for reason of record absent of factual support, and alleges that it self contradictory to argue that the product is different from those made from acetone since none of the form I made in the specification support such an argument. The Examiner further argues that the exclusive disclosure of acetone as the sole solvent for preparing form I (S)-citalopram oxalate is tantamount to a teaching away from using any other solvent absent of factual support.

However, the test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. United States v. Telectronics, Inc., 857 F.2d 778, 785 (Fed. Cir. 1988). A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with

the enablement requirement of 35 USC 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis. In re Marzocchi, 439 F.2d 220, 224 (CCPA 1971). Here, the claims are enabled because there is not any reason to doubt the objective truth of the statements contained in the Specification for enabling support. The Specification discloses the manner and process for making and using the claimed invention, including working examples which show the efficacy of the claimed invention (see ¶[0017], ¶[0018]). For example, the Specification discloses a process of making Form I (S)-citalopram using ethyl acetate, methyl tert-butyl ether, dioxane and acetonitrile (see ¶[0008] and ¶[0009]).

Thus, given the teachings of the Specification, the quantity of experimentation required is not excessive in view of the subject matter of the claims. The Specification sets forth several methods for producing a (S)-citalopram, and the two novel crystalline forms of (S)-citalopram. Working Examples are also provided, as well as detailed information as to the methods. This information can be used by one of ordinary skill in the art to determine appropriate solution conditions to practice the claimed process, without undue experimentation.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

#### **Rejection under 35 USC 102(e)**

Claims 8-9 stand rejected under 35 USC 102(e) as being anticipated by U.S. Patent No. 6,916,941 (Christensen et al.) or alternatively under 35 USC 112 first paragraph as being new matter. This rejection is respectfully traversed.

The Examiner sets forth that were applicants argued that claims 8-9 prepared from methanol or isopropanol is a different material then the ones prepared from ethanol, the new matter rejection is still applicable. If the claims are drawn to material made by alcoholic solvents including ethanol as described in the specification, then the 102(e) rejection is applicable because application disclosed material made using methanol/isopropanol which was disclosed being the same as those made from all other alcohols.

However, while the '941 Christensen patent discloses a method for the manufacture of crystalline particles of (S)-citalopram oxalate by crystallization from ethanol, this is different form the claimed method. In the method of synthesis of Form II (S)-citalopram oxalate of the

instant claims is not dissolved from ethanol or acetone, but from methanol or isopropyl alcohol. In addition, in the method as disclosed in the '941 patent, it was necessary to seed the ethanolic solvent with escitalopram oxalate. This is in contrast to the method as disclosed in the instant application (see Examples 3, 4, and 6), which do not require a seeding step.

With regard to the new matter rejection, as set forth above, the Specification exemplifies the preparation of the claimed form II (S)-citalopram oxalate, therefore no new matter has been added.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

**Rejection under 35 USC 112 first paragraph**

Claims 10-11, 13-14 stand rejected under 35 USC 112 first paragraph as failing to comply with the enablement requirement. This rejection is respectfully traversed.

The Examiner sets forth that no where in the specification have provided evidence that methanol alone without anti-solvent diisopropyl ether will give the form II, and argues that the exclusive disclosure of methanol/di-isopropylether and isopropanol in a field of extreme high degree of experimentation is tantamount to a teaching away from using any other solvent absent of factual support.

However, the claims are enabled because there is not any reason to doubt the objective truth of the statements contained in the Specification for enabling support. The Specification discloses the manner and process for making and using the claimed invention, including working examples which show the efficacy of the claimed invention. For example, the instant application discloses several methods for preparing (see Examples 3, 4, and 6) form II (S)-citalopram oxalate, and the Specification discloses a process of making Form II (S)-citalopram using ethyl acetate, methyl tert-butyl ether, dioxane and acetonitrile (see ¶[0009] and ¶[0010]).

Thus, given the teachings of the Specification, the quantity of experimentation required is not excessive in view of the subject matter of the claims. The Specification sets forth several methods for producing a (S)-citalopram, and the two novel crystalline forms of (S)-citalopram. Working Examples are also provided, as well as detailed information as to the methods. This information can be used by one of ordinary skill in the art to determine appropriate solution conditions to practice the claimed process, without undue experimentation.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

**Rejection under 35 USC 103(a)**

Claims 1-7 stand rejected under 35 USC 103(a) over US 4,943,590 (Boegesoe) in view of Cheronis supplemented with US 6,960,613 (Sanchez et al.), US 6,768,011 (Rock et al.) or US 7,112,686 (Humble et al.) and claims 8-14 stand rejected under 35 USC 103(a) over US 6,916,914 (Christensen et al.) in view of Cheronis supplemented with US 6,960,613 (Sanchez et al.), US 6,768,011 (Rock et al.) or US 7,112,686 (Humble et al.). This rejection is respectfully traversed.

The Examiner sets forth that if applicants argued that form I as now being claims are made by ethyl acetate, methyl t-butyl ether and acetonitrile which is different from the material made by acetone; then, none of the material made by examples 1, 2, or 5 is the claimed material and nowhere in the specification provided antecedent basis or operability of what that is.

The Examiner further sets forth that if applicants argued that changing solvent from acetone to ethyl acetate, methyl t-butyl ether and acetonitrile will produce the same product, then, the 103 (a) rejection is proper since prior art disclosed operability of generic solvents (see p.11 previous office action). The Examiner also sets forth that the same is true for that if applicants argued that form II as now being claims are made by methanol/isopropanol which is different from the material made by ethanol; then, the none of the material made by methanol without antisolvent is the claimed material and nowhere in the specification provided antecedent basis or operability of what that is. The Examiner further argues that if applicants argued that changing solvent from methanol/isopropanol to other alcohol will produce the same product, then, the 103(a) rejection is proper since prior art disclosed operability of generic solvents (see p. 11 previous office action).

The Examiner sets forth that the post application pre-grant application as recited in the previous office action, although are published after the filing date but provided factual support consistent with the teaching of Cheronis supplemented with Sanches and flows naturally with the teaching of the prior art, and that therefore, the posted references are mere evidential support for the obvious conclusion as delineated in the previous office action based on prior art.

However, the claims are patentable over the combination of '590 Boegesoe or '914 Christensen in view of Cheronis supplemented with '613 Sanches, '011 Rock or '686 Humble for the following reasons. To establish a prima facie case of obviousness, three basic criteria must

be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. In re Vaeck, 947 F.2d 488 (Fed. Cir. 1991). MPEP 2143. To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. In re Royka, 490 F.2d 981 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." In re Wilson, 424 F.2d 1382, 1385 (CCPA 1970). MPEP 2143.03. It is important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. (KSR v Teleflex, 12 S.Ct. 1727, 1740 (US 2007)).

Here, not every element of the claims is taught or suggested in the combination of '590 Boegesoe or '914 Christensen in view of Cheronis supplemented with '613 Sanches, '011 Rock or '686 Humble. The instant claims are directed to two novel polymorphs of (S)-citalopram oxalate, and methods of making them. However, the prior art relied upon by the Examiner does not teach or suggest the specific polymorphs as claimed by Applicant. The Examiner failed to demonstrate that there is a known or obvious way to manufacture the specific polymorphic forms claimed.

In addition, there is no motivation for one of skill in the art to alter the methods of the combination of '590 Boegesoe or '914 Christensen in view of Cheronis supplemented with '613 Sanches, '011 Rock or '686 Humble to arrive at the claimed method, and no reasonable expectation of success. The Examiner argues that one having ordinary skill in the art is well aware of all the pertinent art in the field.

However, the '590 Boegesoe patent does not disclose or suggest methods of preparation of (S)-citalopram oxalate crystalline forms wherein the solvent is ethyl acetate, methyl tert-butyl ether, acetonitrile, methanol or isopropyl alcohol. Since the reference does not disclose or suggest this, there is no motivation to employ the process taught by the '590 Boegesoe patent to crystallize (S)-citalopram oxalate and expect to obtain the desired product to reach the

limitations of the claims, with the claimed polymorphic form, and no expectation of success.

While the '590 Boegesoe patent discloses crystallization from acetone (see e.g. Example 2), the instant application discloses that (S)-citalopram oxalate is mixed with acetone, heated to reflux and is cooled to 20°C, then the separated crystals are filtered (see Example 1). As set forth in the Response filed February 12, 2009, the Banga reference teaches that different crystalline modifications arise under varied experimental conditions, including, *inter alia*, thermal treatment.

The deficiencies of the '590 Boegesoe patent are not cured by the addition of the Cheronis supplemented with '613 Sanches, '011 Rock or '686 Humble references. None of the Cheronis, '613 Sanches, '011 Rock or '686 Humble references teaches or suggests the solvent and/or thermal profiles as set forth in the instant application and claims.

While the '941 Christensen patent discloses a method for the manufacture of crystalline particles of (S)-citalopram oxalate by crystallization from ethanol, in the method of synthesis of Form II (S)-citalopram oxalate of the instant claims is not dissolved from ethanol or acetone, but from methanol or isopropyl alcohol. In addition, in the method as disclosed in the '941 patent, it was necessary to seed the ethanolic solvent with escitalopram oxalate. This is in contrast to the method as disclosed in the instant application (see Examples 3, 4, and 6), which do not require a seeding step.

The deficiencies of the '941 Christensen patent are not cured by the addition of the Cheronis supplemented with '613 Sanchez, '011 Rock or '686 Humble references. None of the Cheronis, '613 Sanches, '011 Rock or '686 Humble references teaches or suggests the solvent and/or thermal profiles as set forth in the instant application and claims.

Accordingly, reconsideration and withdrawal of the rejection under 35 USC 103(a) is respectfully requested.

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Application No. 10/509,139  
Amendment Dated 8/25/2009  
Reply to Office Action of 05/07/2009

For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

Should the Examiner believe that anything further is desirable in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

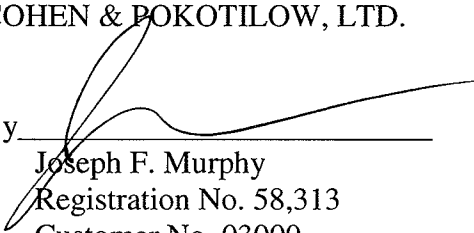
Respectfully submitted,

CAESAR, RIVISE, BERNSTEIN,  
COHEN & POKOTILOW, LTD.

August 25, 2009

Please charge or credit our  
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